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Research paper

Clinical and biochemical aspects associated with diabetic nephropathy among type 2 diabetic males in Gaza strip

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Abstract

Background: Diabetic nephropathy (DN) is the leading cause of end-stage renal disease, and the published data on various aspects of the disease is rare in Gaza Strip.
Objective: to investigate clinical and biochemical aspects associated with DN among type 2 diabetic males in Gaza Strip.
Methods: The study comprised 150 type 2 diabetic males from Gaza Strip. Data were obtained from a questionnaire interview, patients' records, and biochemical analysis of blood and urine samples. Statistical analysis was performed using SPSS version 23.
Results: The prevalence of DN was 71/150 (47.3%). Duration of diabetes in patients with DN was significantly higher than in patients without DN ($p<0.001$). Smoking, retinopathy, cardiovascular diseases (CVD) and neuropathy were significantly more frequent among patients with DN ($p<0.05$). Serum glucose, urea, creatinine, cholesterol and low-density lipoprotein cholesterol (LDL-C) were significantly higher, whereas high-density lipoprotein cholesterol (HDL-C) was significantly lower in patients with DN ($p<0.05$). Urinary albumin and Albumin/creatinine ratio (ACR) were 10 to 13 times higher in patients with DN. Conversely, glomerular filtration rate (GFR) was significantly lower in patients with DN (137.1±35.0 versus 187.8±70.8 ml/min/1.73m^2, $p<0.001$). ACR showed significant positive correlations with duration of diabetes ($r=0.311$, $p<0.001$), glucose ($r=0.308$, $p<0.001$), urea ($r=0.474$, $p<0.001$), creatinine ($r=0.356$, $p<0.001$), cholesterol ($r=0.307$, $p<0.001$), LDL-C ($r=0.319$, $p<0.001$) and urinary albumin ($r=0.942$, $p<0.001$), and significant negative correlation with GFR ($r=-0.297$, $p<0.001$). The predicted factors of DN were duration of diabetes, smoking, retinopathy, CVD, neuropathy, glucose, urea, creatinine, cholesterol, LDL-C and GFR. The more to fewer effective predicted variables of ACR were urinary albumin, urea, creatinine, LDL-C, duration of diabetes, glucose, cholesterol and GFR.
Conclusion: Management of some predicted factors of DN could delay the progression of the disease.

Keywords: *Diabetic Nephropathy; Clinical and Biochemical Aspects; Gaza Strip.*

1. Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (American Diabetes Associations, 2014). The main types of diabetes are insulin dependent (type 1) and non-insulin dependent (type 2) diabetes. Type 2 diabetes is much more common than type 1 and usually begins as insulin resistance, a disorder in which the cells do not respond properly to insulin (Ozougwu et al. 2013). Reduce peripheral insulin sensitivity with increased hepatic glucose output resulting in the development of hyperglycemia (König & Holzhütter 2012). Additionally, high levels of circulating fatty acids due to promotion of lipolysis, elevated levels of triglycerides, cholesterol and LDL-C with low levels of HDL-C were recognized in type 2 diabetic patients (Abd El-Azim et al. 2013; Sabahelkhier et al. 2016).
The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. DN is one of the most severe chronic complications of diabetes and is characterized by an increased urinary albumin excretion in the absence of other renal diseases (Yassin et al. 2011; Bennett and Aditya 2015). Microalbuminuria or incipient nephropathy is the earliest clinical evidence of DN (ACR of 30-300 mg/g, equivalent to timed collections of 30-300 mg/24 hours). Progression to macroalbuminuria or overt nephropathy is heralded by a urinary albumin excretion of > 300 mg/24 hours or ACR > 300 mg/g and is more likely to be associated with the development of end-stage renal disease (Reutens 2013; Lim 2014).
In addition to albuminuria, GFR was identified as the other diagnostic modality of DN (Tuttle et al. 2014; Kim et al. 2016). The GFR is considered to be the most reliable measure of the functional capacity of the kidneys and is often thought of as indicative of the number of functioning nephrons. It has been proved to be the most sensitive and specific marker of changes in overall renal function (Burtis et al. 2006). A low or decreasing GFR is a good index of chronic kidney disease. Since the total kidney GFR is equal to the sum of the filtration rates in each of the functioning nephrons, the total GFR can be used as an index of functioning renal mass. A decrease in GFR precedes kidney failure in all forms of progressive kidney disease. Monitoring changes in GFR can delineate progression of kidney disease (Krishnaswamy & Lukose 2015).
Although DN is difficult to capture in the earliest stage because loss of signs and symptoms, its global prevalence is estimated to vary between 5% and 30% in patients with type 2 diabetes and microalbuminurea are present in about 40% of the subjects after 10 years of evolution. The risk of a progressive increase in albumin excretion to overt proteinuria within 6-14 years was 60-80%

(Ritz Zeng 2011; Ono et al. 2014; Zenteno-Castillo et al. 2015). In Gaza Strip, thereares no real figures on the prevalence of DN and even researchinton the disease is lacking and restricted to few annual unpublished reports emerged from the Palestinian Ministry of Health. To our best knowledge, the present study is the first to assess clinical and biochemical aspects associated with DN among type 2 diabetic males in Gaza Strip. Understanding such aspects could be useful in the management of the disease.

2. Methodology

2.1. Study design and study population

The present study was a cross-sectional study. The study population comprised 150 types 2 diabetic males (40-60 years old) who were previously diagnosed according to the current World Health Organization diagnostic criteria for diabetes (World Health Organization, WHO 2006). The patients were selected randomly from the five Diabetic Clinics in the five Governorates of the Gaza Strip, which are the representative clinics for diabetic patients in Gaza Strip, distributed as follows: North 30 (20.0%), Gaza 50 (33.3%), Mid-zone 22 (14.7%), Khan Yunis 30 (20.0%) and Rafah 18 (12.0%). Patients who have urinary tract infection were excluded.

2.2. Ethical consideration

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Local Ethics Research Committee. All subjects provided written informed consent prior to the study.

2.3. Questionnaire interview

A meeting interview was used for filling in the questionnaire. All interviews were conducted face to face by one investigator who had a Master degree of Medical Technology. The questionnaire was based on diabetic clinic questions of the Palestinian Ministry of Health with some modifications (Palestinian Ministry of Health 2006). Most questions were the yes/no type, which offer a dichotomous choice (Backestrom & Hursh-Cesar 2012). A questionnaire was piloted with 10 patients not included in the population sample, and modified as necessary. The questionnaire included questions related to age, smoking, family history of diabetes and diet.

2.4. Patients' records

Clinical data including duration of diabetes and diagnosed diabetic complications were obtained from the patients' records.

2.5. Body mass index

The body weight and height of each individual dressed in light clothing without shoes were measured using a carefully calibrated balance (Detecto, CAP-180 Kg, USA) for weight and vertical measuring rod for height. The BMI was calculated as Kg body weight/height in meter squared. People with BMI=18.5-24.9 were considered to have normal weight; people with BMI=25.0-29.9 were classified overweight and people with BMI ≥ 30.0 were considered obese (WHO 2014).

2.6. Blood and urine sampling and processing

Fasting overnight venous blood samples (about 8 ml each) were collected into vacutainer tubes from 150 type 2 diabetic patients by a well-trained medical technologist. The blood samples were left for a while without anticoagulant to allow blood to clot. Then, serum samples were obtained by centrifugation at room temperature using Rotina 46 Hettich Centrifuge, Japan at 4000 rpm/10 minutes to be used for biochemical analysis. Random urine samples were also collected from the patients. The samples were then centrifuged by the same way as serum to precipitate all the debris and then used for urine analysis. For urinary creatinine determination, urine samples were diluted 1/20 (25 urine/475 distilled water).

2.7. Biochemical analysis

Serum glucose was measured by glucose oxidase (GOD)/glucose peroxidase (POD) method using Labkit Kits, Spain (Trinder 1969). Serum urea and creatinine were determined by urease-glutamate dehydrogenase (GDH)/UV method and by Alkaline Picrate method, respectively using BioSystems kit, Spain (Bergmeyer 1974; Fabiny & Ertingshausen 1971). Serum cholesterol and triglycerides were measured by cholesterol oxidase (COD)/POD method and by glycerol phosphate oxidase/peroxidase method, respectively using BioSystems kit, Spain (Meiatlini et al. 1978; Bucolo & David 1973). High-density lipoprotein cholesterol (HDL-C) was determined by precipitating method using Labkit kit, Spain (Grove 1979). Low-density lipoprotein cholesterol (LDL-C) was calculated using the empirical relationship of Friedewald (Friedewald et al. 1972).

2.8. Urine analysis

Urinary albumin was determined by Immunoturbidometry-Latex method using BioSystems kit, Spain (Harmoinen et al. 1985). Urinary creatinine was measured by kinetic test without deproteinization using DiaSys reagent kits (Bartels et al. 1972). ACR (mg/g) = microalbumin in urine (mg/L) x1000 /creatinine in urine (mg/dl) x10. The urine creatinine value was multiplied by 10 in order to convert mg/dL into mg/L, then divide the urine albumin value by the urine creatinine value to arrive at the ratio, then the ratio was multiplied by 1000 to express the value as (mg albumin/g creatinine). GFR was calculated by Schwartz equation: GFR (ml/min/1.73m^2) = 0.55 x length / serum creatinine.

2.9. Data analysis

Data entry and statistical analyses were performed using Statistical Package for Social Sciences Inc, Chicago, Illinois (SPSS) computer program version 23 for windows. Simple distribution over the study variables and the cross tabulation were applied. Chi-square (χ^2) was used to identify the significance of the relations between various variables. Means were compared by independent-samples t-test. Pearson's correlation test was applied. Logistic and multiple linear regressions by backward stepwise method were also applied to build model to predict diabetic nephropathy of type 2 diabetes and to predict ACR of studied factors. The results in all the above-mentioned procedures were accepted as statistically significant when the P-value was less than 5% ($p<0.05$). Range as minimum and maximum values was used. The percentage difference was calculated according to the formula: Percentage difference equals the absolute value of the change in value, divided by the average of the 2 numbers, all multiplied by 100. Percent difference = (| (V1 - V2) | / ((V1 + V2)/2)) * 100.

3. Results

The mean age of diabetic patients (n=150) was 50.6±6.2 years and the mean duration of diabetes was 7.0±5.8 years. Diabetic patients since ≤ 5 years were 76 (50.7%), whereas those with diabetic duration of 6-10 years were 42 (28.0%). The rest of patients 32 (21.3%) had diabetes for more than 10 years. The main diagnosed complications among diabetic patients were retinopathy 36 (24.0%), cardiovascular diseases 15 (10.0%) and neuropathy 15 (10.0%). According to ACR, our study population (150 type 2 diabetic patients) were classified into 71 (47.3%) patients with DN (ACR ≥ 30 mg/g) and 79 (52.7%) patients without DN (ACR < 30 mg/g).

3.1. General characteristics of diabetic patients with and without DN

As indicated in Table 1, there were no significant differences between patients with and without DN in terms of age, BMI, family history of diabetes and diet (p>0.05). However, the number of smoker patients with DN 23 (32.4%) were significantly higher than that of smoker patients without DN 9 (11.4%) with χ^2 = 9.828 and p=0.002, indicating that DN is associated with smoking.

Table 1: General Characteristics of Diabetic Patients with and Without DN

Characteristic	Diabetic patients (n=150) With DN (n =71)	Without DN (n=79)	test		p-value
Age±SD (years)	51.3±6.5	50.0±5.9	t	1.246	0.215
(Min - max)	(40-60)	(40-60)			
BMI±SD (kg/m^2)	30±4.8	30.5±9.8	t	-0.388	0.699
(Min - max)	(20-42)	(19-109)			
Smoking					
Yes	23 (32.4)	9 (11.4)	χ^2	9.828	0.002
No	48 (67.6)	70 (88.6)			
Family history					
Yes	47 (66.2)	43 (54.4)	χ^2	2.157	0.142
No	24 (33.8)	36 (45.6)			
Diet					
Yes	29 (40.8)	36 (45.6)	χ^2	0.340	0.560
No	42 (59.2)	43 (54.4)			

DN: Diabetic Nephropathy. BMI: Body Mass Index. People with BMI=18.5-24.9 were considered to have normal weight, people with BMI=25.0-29.9 were classified overweight and people with BMI ≥ 30.0 were considered obese (WHO 2014). Values are n (%) except age and BMI where values are expressed as means±SD. p < 0.05: Significant, p > 0.05: Not significant.

3.2. Duration of diabetes and diabetic complications among diabetic patients with and without DN

Table 2 revealed that the mean duration of diabetes in patients with DN was significantly higher than that in patients without DN (10.3±6.0 versus 4.0±3.5 years, p<0.001). The percentage of retinopathy, CVD and neuropathy in patients with DN was significantly higher than that in patients without DN (32.4, 18.3 and 15.5% versus 17.7, 2.5 and 5.1% with p=0.037, p=0.001 and p=0.034, respectively), implying that DN is associated with retinopathy, CVD and neuropathy.

Table 2: Duration of Diabetes and Diabetic Complications among Diabetic Patients with and Without DN

Characteristic	Diabetic patients (n=150) With DN (n =71)	Without DN (n=79)	test		p-value
Duration of diabetes±SD (year)	10.3±6.0	4.0±3.5	t	7.962	<0.001
(Min - max)	(1-25)	(1-17)			
Retinopathy					
Yes	23 (32.4)	14 (17.7)	χ^2	4.332	0.037
No	48 (67.6)	65 (82.3)			
CVD					
Yes	13 (18.3)	2 (2.5)	χ^2	10.343	0.001
No	58 (81.7)	77 (97.5)			
Neuropathy					
Yes	11 (15.5)	4 (5.1)	χ^2	4.520	0.034
No	60 (84.5)	75 (94.9)			

DN: Diabetic Nephropathy. CVD: cardiovascular diseases. Values are n (%) except duration of diabetes where values are expressed as means±SD. p < 0.05: Significant.

3.3. Serum glucose, urea, creatinine and lipid profile of diabetic patients with and without DN

As illustrated in Table 3, serum glucose was significantly increased in patients with DN compared to patients without DN (238.7±80.6 versus 126.1±35.5 mg/dl, % difference = 61.7 and p<0.001). Similarly, serum urea, creatinine, cholesterol and LDL-C in patients with DN (29.0±7.0, 0.73±0.16, 206.9±41.6 and 117.3±40.9) mg/dl, respectively) were significantly higher than that in patients without DN (20.3±7.0, 0.56±0.18, 190.6±34.4 and 102.3±31.7 mg/dl, respectively) with % differences of 35.3, 26.4, 8.2 and 13.7 and p-values of <0.001, <0.001, 0.009 and 0.012, respectively. Serum triglycerides were also increased in patients with DN but without significant change (p=0.166). Conversely, serum HDL-C was significantly lower in patients with DN than patients without DN (41.4±5.3 versus 44.3±6.8 mg/dl) with % difference of 6.8 and p=0.004).

3.4. Urinary albumin, creatinine, ACR and GFR of diabetic patients with and without DN

Table 4 provides urinary albumin and creatinine concentrations as well as ACR and GFR of diabetic patients with and without DN. Urinary albumin concentration was several folds higher in patients with DN than patients without DN (201.7±204.2 versus 18.3±12.7 mg/dl, % difference = 166.7, p<0.001). However, there was no significant difference in urinary creatinine between patients with and without DN (p=0.254). Consequently, ACR was several folds higher in patients with DN than patients without DN (215.7±216.7 versus 16.0±7.8 mg/g, % difference = 172.4, p<0.001). Conversely, GFR was significantly lower in patients with DN than patients without DN (137.1±35.0 versus 187.8±70.8 ml/min/1.73m^2, % difference = 31.2, p<0.001).

3.5. ACR in relation to the studied parameters of both patients with and without DN (n=150)

Correlations between ACR and the studied parameters of both patients with and without DN are pointed out in Table 5. Pearson correlation coefficient test showed significant positive correlations of ACR with duration of diabetes (r=0.311, p<0.001), glucose (r=0.308, p<0.001), urea (r=0.474, p<0.001), creatinine (r=0.356, p<0.001), cholesterol (r=0.307, p<0.001), LDL-C (r=0.319, p<0.001) and urinary albumin (r=0.942, p<0.001), and significant negative correlation with GFR (r=-0.297, p<0.001) in both patients with and without DN. However, ACR exhibited no significant correlations with age, BMI, triglycerides, HDL-C and urinary creatinine.

3.6. Logistic regression model for independent variables to predict DN

As depicted from Table 6, the adjusted odd ratios with 95% CI for all independent variables revealed that the predicted factors of DN among type 2 diabetic patients in Gaza Strip were duration of diabetes [OR=1.321, 95% CI (1.200-1.454), p<0.001], smoking [OR=3.727, 95% CI (1.587-8.752), p=0.003], retinopathy [OR=2.225, 95% CI (1.038-4.766), p=0.040], CVD [OR=8.629, 95% CI (1.874-39.740), p=0.006], neuropathy [OR=3.437, 95% CI (1.042-11.341), p=0.043], glucose [OR=1.042, 95% CI (1.028-1.057), p<0.001], urea [OR=1.233, 95% CI (1.143-1.330), p<0.001], creatinine [OR=461.835, 95% CI (38.731-5507.0), p<0.001], cholesterol [OR=1.012, 95% CI (1.003-1.021), p=0.012], LDL-C [OR=1.012, 95% CI (1.002-1.021), p=0.015], and GFR [OR=0.979, 95% CI (0.970-0.988), p<0.001].

3.7. Multiple linear regression model to predict ACR of diabetic patients

As shown in Table 7, multiple linear regression analysis demonstrated that the predict variables from more to less effective to predict ACR were urinary albumin [t=34.242, p<0.001], urea [t=6.551, p<0.001], creatinine [t=4.630, p<0.001] LDL-C, [t=4.091, p<0.001], duration of diabetes [t=3.985, p<0.001], glucose [t=3.941, p<0.001], cholesterol [t=3.917, p<0.001] and GFR [t=-3.784, p<0.001].

Table 3: Serum Glucose, Urea, Creatinine and Lipid Profile of Diabetic Patients with and Without DN

Variable	Diabetic patients (n=150) With DN (n =71)	Without DN (n=79)	% difference	t-test	p-value
Glucose (mg/dl) (Min – max)	238.7±80.6 (75-460)	126.1±35.5 (72-217)	61.7	11.270	<0.001
Urea (mg/dl) (Min – max)	29.0±7.0 (12-59)	20.3±7.0 (8-40)	35.3	7.572	<0.001
Creatinine (mg/dl) (Min – max)	0.73±0.16 (0.3-1.4)	0.56±0.18 (0.2-1.1)	26.4	5.948	<0.001
Cholesterol (mg/dl) (Min – max)	206.9±41.6 (116-315)	190.6±34.4 (88-276)	8.2	2.636	0.009
Triglycerides (mg/dl) (Min – max)	243.1±108.9 (66-759)	220.1±93.2 (79-650)	9.9	1.393	0.166
HDL-C (mg/dl) (Min – max)	41.4±5.3 (28-54)	44.3±6.8 (31-89)	-6.8	-2.937	0.004
LDL-C (mg/dl) (Min – max)	117.3±40.9 (27-222)	102.3±31.7 (29-185)	13.7	2.541	0.012

DN: Diabetic Nephropathy. HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol. All values are expressed as mean±SD. $p < 0.05$: Significant, $p > 0.05$: Not significant.

Table 4: Urinary Albumin, Creatinine, ACR and GFR of Diabetic Patients with and Without DN

Variable	Diabetic patients (n=150) With DN (n =71)	Without DN (n=79)	% difference	t-test	p-value
Urinary Albumin (mg/dl) (Min - max)	201.7±204.2 (18-1063)	18.3±12.7 (3-79)	166.7	7.970	<0.001
Urinary creatinine (mg/dl) (Min - max)	99.0±50.3 (28-347)	107.3±38.2 (22-232)	-8.0	-1.144	0.254
ACR (mg/g) (Min - max)	215.7±216.7 (31-1328)	16.0±7.8 (1.9-29)	172.4	7.761	<0.001
GFR (ml/min/1.73m²) (Min - max)	137.1±35.0 (61-317)	187.8±70.8 (72-473)	-31.2	-5.467	<0.001

DN: Diabetic Nephropathy. ACR: Albumin/creatinine ratio, GFR: Glomerular filtration rate. All values are expressed as mean±SD. $p < 0.05$: Significant, $p > 0.05$: Not significant.

Table 5: ACR In Relation To the Studied Parameters of Both Patients with and Without DN

Parameter	ACR (mg/g) (n=150) r	p-value
Age (years)	0.034	0.676
Duration of diabetes (Year)	0.311	<0.001
BMI (kg/m²)	-0.029	0.727
Glucose (mg/dl)	0.308	<0.001
Urea (mg/dl)	0.474	<0.001
Creatinine (mg/dl)	0.356	<0.001
Cholesterol (mg/dl)	0.307	<0.001
Triglycerides (mg/dl)	0.049	0.552
HDL-C (mg/dl)	-0.153	0.061
LDL-C (mg/dl)	0.319	<0.001
Urinary Albumin (mg/dl)	0.942	<0.001
Urinary creatinine (mg/dl)	-0.085	0.304
GFR (ml/min/1.73m²)	-0.297	<0.001

ACR: Albumin/creatinine ratio, r: correlation coefficient, BMI: Body Mass Index, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol, GFR: Glomerular filtration rate. The correlation was analyzed using Pearson correlation coefficient (normally distributed data). $p < 0.05$: Significant, $p > 0.05$: Not significant.

Table 6: Logistic Regression Model for Independent Variables to Predict DN

Factor	B	S.E.	Wald	p-value	Odds*	95% CI for OR Lower	Upper
Duration of diabetes (Year)	0.278	0.049	32.402	< 0.001	1.321	1.200	1.454
Smoking	1.316	0.436	9.123	0.003	3.727	1.587	8.752
Retinopathy	0.800	0.389	4.231	0.040	2.225	1.038	4.766
CVD	2.155	0.779	7.650	0.006	8.629	1.874	39.740
Neuropathy	1.235	0.609	4.110	0.043	3.437	1.042	11.341
Glucose (mg/dl)	0.042	0.007	35.496	< 0.001	1.042	1.028	1.057
Urea (mg/dl)	0.209	0.039	29.279	< 0.001	1.233	1.143	1.330
Creatinine (mg/dl)	6.135	1.265	23.537	< 0.001	461.835	38.731	5507.0
Cholesterol (mg/dl)	0.012	0.005	6.381	0.012	1.012	1.003	1.021
LDL-C (mg/dl)	0.012	0.005	5.952	0.015	1.012	1.002	1.021
GFR (ml/min/1.73m²)	-0.021	0.005	19.541	< 0.001	0.979	0.970	0.988

*Adjusted Odd Ratio, CVD: Cardiovascular disease, LDL-C: Low density lipoprotein cholesterol, GFR: Glomerular filtration rate. $p < 0.05$: Significant.

Table 7: Multiple Linear Regression Model to Predict ACR (Mg/G) Of Diabetic Patients

Predictors	B	SE	t	p-value	95% CI for B	
					Lower	Upper
Urinary Albumin (mg/dl)	1.007	0.029	34.242	<0.001	0.949	1.065
Urea (mg/dl)	10.289	1.571	6.551	<0.001	7.185	13.393
Creatinine (mg/dl)	339.169	73.256	4.630	<0.001	194.407	483.932
LDL-C (mg/dl)	1.544	0.377	4.091	<0.001	0.798	2.290
Duration of diabetes (Year)	9.665	2.425	3.985	<0.001	4.873	14.458
Glucose (mg/dl)	0.665	0.169	3.941	<0.001	0.332	0.999
Cholesterol (mg/dl)	1.417	0.362	3.917	<0.001	0.702	2.131
GFR (ml/min/1.73m²)	-0.859	0.227	-3.784	<0.001	-1.307	-0.410

ACR: Albumin/creatinine ratio, LDL-C: low density lipoprotein cholesterol, GFR: Glomerular filtration rate. B: regression coefficient, SE: standard errors. $p < 0.05$: Significant.

4. Discussion

Type 2 diabetes mellitus is being increased in Gaza strip, particularly in the last decade. However, no real figures are available on its prevalence and its complications. In fact, there is a scarcity of data on the development of the disease towards DN evident by micro- and/or macroalbuminurea. Only one published study related diabetes with DN in type 2 diabetic patients in Gaza strip (Yassin et al. 2011). Recently, another study has recognized diabetes mellitus as one of the most common risk factor associated with end-stage renal disease in Gaza Strip (Abu-Odah et al. 2016). This necessitates further research on various features of DN. Therefore, the present study is the first to assess the frequency of DN among a population sample of type 2 diabetic males in Gaza Strip as well as to investigate clinical and biochemical aspects associated with DN not only in blood but also in urine to get a clear and broad picture on patient condition, and to help in the disease management.

The mean age within the study population (type 2 diabetic patients) was 50.6±6.2 years, which coincides with the fact that type 2 diabetes mellitus usually develops at older age (Bhalerao et al. 2014). The finding that almost half of the study population had diabetes for 5 years or less does confirm the idea that type 2 diabetes has a long asymptomatic pre-clinical phase which frequently goes undetected. At the time of diagnosis, the patient could have one or more diabetes complications (Shaikh et al. 2008; Yassin et al. 2011). Indeed, retinopathy, CVD and neuropathy were the main diagnosed complications among our diabetic patients. We then moved one step ahead depending on ACR and classified diabetic patients into patients with DN (ACR ≥ 30 mg/g) and patients without DN (ACR < 30 mg/g). This enable us to assess various aspects of DN in type 2 diabetic patients.

The prevalence of DN among our population sample of 150 type 2 diabetic patients was 47.3%. There was no previous study assessed the prevalence of DN in Gaza Strip neither at a small nor at a large diabetic population scale. Nevertheless, our figure of DN prevalence coincides with that previously reported (Prakash et al. 2006; Ono et al. 2014). Further research is required on a large sample size at a national level. There were no significant differences between patients with and without DN in terms of age, BMI, family history of diabetes and diet. However, DN was associated with smoking. It is accepted that smoking promotes diabetic microalbuminuria and exacerbates DN (Jose et al. 2016).

The present data pointed out that the mean duration of diabetes in patients with DN was significantly higher than that in patients without DN i.e. the longer the duration of diabetes, the more the progression of DN. Similar results were documented (Viswanathan et al. 2012; Radcliffe et al. 2017). In addition, diagnosed complications, including retinopathy, CVD and neuropathy were significantly more frequent in patients with DN than in patients without DN. This means that DN is associated with higher rate of retinopathy, cardiovascular diseases and neuropathy. Such findings are in accordance with that reported by other authors (Pálsson & Patel 2014; Bennett & Aditya 2015; Rodríguez-Poncelas et al. 2016). In this context, the development of such complications particularly CVD would be accelerated and exacerbated in smoker patients with DN.

Serum glucose, urea, creatinine, cholesterol and LDL-C were significantly higher in patients with DN compared to patients without DN. Conversely, serum HDL-C was significantly lower in patients with DN. Such findings are in agreement with that reported in the literature (Kumawat et al. 2016; Vinoth et al. 2016). The higher levels of serum urea and creatinine in the presence of hyperglycemia in patients with DN indicate progressive renal damage and kidney dysfunction (Bamanikar et al. 2016). Dyslipidemia observed in the present study is also reported to be associated with decreased kidney function in patients with chronic kidney disease (Kawanami et al. 2016). It is worth mentioning that DN plays a critical role as a risk factor for CVD and altered lipid levels will increase the risk. The higher rate of diagnosed CVD among our DN patients does support this view. Therefore, baseline lipid profile during screening programmes for diabetes and monitoring their levels is beneficial.

Urinary albumin concentration and consequently, ACR was several folds higher in patients with DN than patients without DN. Conversely, GFR was significantly lower in patients with DN. Elevation of urinary albumin concentration and hence ACR as well as decrease GFR in DN patients were documented by other authors and explained mostly as a result of impairment of kidney filtration efficiency (Jerums et al. 2009; Lee & Lam 2015). Thus, we can say that both albuminuria and GFR are integrating biomarkers in screening, diagnosis and monitoring of DN. This is very important as these tests are relatively cheaper and therefore, more affordable compared with other diagnostic tests such as magnetic resonance imaging, computerized tomography scan, which are more expensive and may not be readily affordable by the majority of people in poor areas such as Gaza Strip.

As depicted from Pearson's correlation test, ACR showed significant positive correlations with duration of diabetes, glucose, urea, creatinine, cholesterol, LDL-C and urinary albumin, and significant negative correlation with GFR in both patients with and without DN. Similar findings were reported for other studies (Adewolu & Atoe 2015; Vinoth et al. 2016; Abbas et al. 2017). Such associations could be used as indicators for the progression of diabetes to DN and even to end-stage renal disease. In this context, logistic regression model revealed that the predicted factors of DN were duration of diabetes, smoking, retinopathy, CVD, neuropathy, glucose, urea, creatinine, cholesterol, LDL-C and GFR. Most of these factors were identified as clinical and biochemical predictive factors in diabetic kidney disease progression (Grover et al. 2012; Radcliffe et al. 2017). However, the exact stage of DN is beyond the scope of this study. In addition, Multiple linear regression model demonstrated that the predict variables from more to less effective to predict ACR was urinary albumin, urea, creatinine, LDL-C, duration of diabetes, glucose, cholesterol and GFR.

In conclusion, the prevalence of DN among diabetic patients in Gaza Strip seems to be alarming. The predicted factors of DN were duration of diabetes, smoking, retinopathy, CVD, neuropathy, glucose, urea, creatinine, cholesterol, LDL-C and GFR. Management of some of these factors could delay the progression of DN.

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